ABSTRACT OF THE DISCLOSURE

To identify molecular determinants of lytic bone disease in multiple myeloma, the expression profiles of ~12,000 genes in CD138-enriched plasma cells from newly diagnosed multiple myeloma patients exhibiting no radiological evidence of lytic lesions (n = 28) were compared to those with ≥ 3 lytic lesions (n = 47). Two secreted WNT signaling antagonists, soluble frizzled related protein 3 (SFRP-3/FRZB) and the human homologue of Dickkopf-1 (DKK1), were expressed in 40 of 47 with lytic bone lesions, but only 16 of 28 lacking bone lesions ($P < .05$). DKK1 and FRZB were not expressed in plasma cells from 45 normal bone marrow donors or 10 Waldenstrom's macroglobulinemia, a related plasma cells malignancy that lacks bone disease. These data indicate that these factors are important mediators of multiple myeloma bone disease, and inhibitors of these proteins may be used to block bone disease.